REMARKS

Status of the Claims.

Claims 1-9, 12-18, and 20-26 are pending with entry of this amendment, claims 10, 11, and 19 being cancelled and no claims being added herein. Claims 1, 6, 9, 12-18, and 21-26 are amended herein. These amendments introduce no new matter. Support is replete throughout the specification (*e.g.,* in the claims as originally filed).

35 U.S.C. §112, Second Paragraph.

Claims 1-9, 12-18, and 20-26 were rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite because of the phrase "synergistic combination". The claims are amended herein to eliminate the term "synergistic combination" thereby obviating this rejection.

35 U.S.C. §103(a).

Claims 1-6, 9, 11-22, and 24-34 were rejected under 35 U.S.C. §103(a) as allegedly obvious in light of Yu *et al.* (U.S. Patent 5,385,938), in view of Poli *et al.* (1979) *Food Chemistry*, 4(3): 251-258, Wenninger (International Cosmetic Ingredient Dictionary and Handbook, 7th Ed., 1: 163-168, Merck Index 11th ed. (1989) Glycolic acid monograph 4394, page 439), and Pamukoff (Canadian Patent 1, 221,640). According to the Examiner, Yu *et al.* teaches a topical composition with glycolic acid as the active ingredient and ethanol as the solvent. Poli *et al.* is cited as allegedly teaching that glycolic acid is virucidal against herpesvirus. Wenninger is cited as allegedly teaching that butylenes glycol is useful as a solvent in numerous cosmetic marketed products. The Merck index allegedly teaches that the pH of 0.5% glycolic acid solution is 2.50. Pamukoff allegedly teaching the use of 1-10% ethyl alcohol containing compositions for treating viral infections broadly. Applicants traverse.

As reiterated by the Supreme Court in(*KSR International Co. v. Teleflex Inc.* 127 S.Ct. 1727, 167 L.Ed.2d 705, 75 USLW 4289, 82 USPQ2d 1385 (2007), the framework for the objective analysis for determining obviousness under 35 U.S.C. 103 is stated in *Graham* v. *John Deere Co.* 383 U.S. 1, 148 USPQ 459 (1966). Obviousness is a question of law based on underlying factual inquiries. The factual inquiries enunciated by the Court are as follows:

(1) Determining the scope and content of the prior art;

(2) Ascertaining the differences between the claimed invention and the prior art;

(3) Resolving the level of ordinary skill in the art; and

(4) Evaluating any evidence of secondary considerations.

However as recognized in the Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in KSR *International Co.* v. *Teleflex Inc.* Federal Register 72(195), at 5279:

> **When the prior art teaches away from combining certain known elements, discovery of successful means of combining them is more likely to be nonobvious**." [emphasis added]

In addition, the Examiner is also reminded that the MPEP expressly states that "**if the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification**. MPEP §2143.01, *citing In re Gordon*, 221 USPQ 1125 (Fed. Cir. 1984).

In the instant case, modification of the compositions of Yu *et al.* would make the formulation unsatisfactory for Yu et al.'s intended purpose. Moreover, Yu *et al.* expressly teach away from the presently claimed formulation. In particular, Yu *et al.* teach the use of compositions containing **both**:

1) an **amphoteric or pseudoamphoteric** compound; and
2) **alpha hydroxyacids, alpha ketoacids** or related compound.

Thus, for example, Yu *et al.* expressly states:

> It has now been discovered that **amphoteric compositions** containing alpha hydroxyacids, alpha ketoacids or related compounds, and also the compositions containing dimeric or polymeric forms of hydroxyacids overcome the aforementioned shortcomings and retain the therapeutic efficacies for cosmetic conditions and dermatologic disorders. **The amphoteric composition contains in combination an amphoteric or**

> **pseudoamphoteric compound and at least one of the alpha hydroxyacids, alpha ketoacids or related compounds**. [emphasis added] (col. 3, lines 10-12).,
>
> The amphoteric composition of the instant invention contains in combination an **alpha hydroxyacid or alpha ketoacid and an amphoteric or pseudoamphoteric compound**. [emphasis added]

This is illustrated by Example 1 (col. 14, lines 1-10) which states:

> An amphoteric composition containing 1M **2-hydroxyethanoic acid and 0.5M L-arginine** in solution form for dandruff or dry skin may be formulated as follows.
> 2-Hydroxyethanoic acid (glycolic acid) 7.6 g is dissolved in water 60 ml and propylene glycol 20 ml. **L-Arginine 8.7 g is added to the solution** with stirring until all the crystals are dissolved. Ethanol is added to make a total volume of the solution to 100 ml. The amphoteric composition thus formulated has pH 3.0. An amphoteric composition formulated from 1M 2-hydroxyethanoic acid and 1M L-arginine has pH 6.3. **The solution has pH 1.9 if no amphoteric compound is incorporated.** [emphasis added]

In this instance, 2-hydroxyethanoic acid is the alphahydroxy acid, while **L-arginine is the amphoteric compound**. *See, e.g.,* col.5, lines 1-7 which state:

> The **representative amphoteric compounds of amino acid type may be listed as follows: Glycine**, alanine, valine, leucine, isoleucine, serine, threonine, cysteine, cystine, methionine, aspartic acid, asparagine, glutamic acid, glutamine, arginine, lysine, 5-hydroxylysine, histidine, phenylalanine, tyrosine, tryptophan, 3-hydroxyproline, 4-hydroxyproline and proline. [emphasis added]

Elimination of the L-arginine (the amphoteric compound) to produce a composition consisting of glycolic acid and ethanol would defeat the central teaching of the Yu *et al.* patent. Moreover, Yu *et al.* expressly teaches that in the absence of the amphoteric compound, the solution has a pH of 1.9 which is lower than the pH of 2.45 to 4.5 recited in the pending claims.

Yu *et al.* thus, by teaching the necessity of an amphoteric or pseudoamphoteric compound, expressly leads one of skill away from the presently claimed invention. Moreover, elimination of the amphoteric compound would defeat the central teaching of Yu *et al.* and render their compounds unsuitable for the intended use.

Yu *et al.* thus fails to teach or suggest the presently claimed invention and expressly teaches away. The defects of Yu *et al.* are not remedied by Poli *et al.* Wenninger, the Merck Index, or Pamukoff.

For example, Poli *et al.* allegedly teaches that glycolic acid is virucidal against herpesvirus **in culture.** Poli *et al.* offers no teaching or suggestion of treating an inflammation or lesion. In addition, Poli *et al.* offers no teaching or suggestion of the combination of glycolic acid and an alcohol as presently claimed. Moreover combination of the teaching of Poli *et al.* with Yu *et al.* to produce the presently claimed method would still require elimination of the amphoteric compound and thus render the compounds of Yu *et al.* unsuitable for their intended use.

The Merck index, cited by the Examiner expressly states:

> Use: In the processing of textiles, leather, and metals; in pH control, and wherever a cheap organic acid is needed, *e.g.*, in the manuf of adhesives, in copper brightening, decontamination cleaning, dyeing, electroplating, in pickling, cleaning and chemical milling of metals. ***Caution:*** **Mild irritant to skin, mucous membranes.**

By teaching that glycolic acid is an irritant, the Merck index leads one of skill away from the use of glycolic acid in topical applications, **particularly for the treatment of lesions as recited in the pending claims**. The combination of Yu *et al.*, Poli *et al.*, and/or the Merck Index, simply offers no teaching or suggestion of the presently claimed invention and, in fact teaches away from such an invention.

The defects of these references are not remedied by Wenninger or Pamukoff.

Pamukoff teaches pharmaceutical compositions comprising glycerine, ethyl alcohol, **and an alkali metal halide salt**:

> Thus according to one aspect of the present invention, there is provided a pharmaceutical composition for use in topical application to alleviate virus infections of the herpes family of viruses and common cold virus, which comprises from about **2.5 to 5.0 parts, by weight of glycerine**, from about 1 to about 10 parts by weight of ethyl alcohol, and from 0 to about 1 part by weight of a physicologically acceptable **alkali metal halide** salt. [emphasis added (page 2, paragraph 2)

* * *

> Preferably such formulations are proivded in a pharmaceutically acceptable carrier base. . . . a suitable amount of water for use with the above-formualtion being from about 80 to about 120 parts by wieght. (page 2, 3rd paragraph).

Pamukoff thus teaches the necessity of a halide salt. Moreover, as indicated above, both the glycerine and the halide salt are regarded as active ingredients, not a pharmaceutically acceptable carrier base. By teaching the requirement of a halide salt and by offering no teaching or suggestion of the presently claimed combination of alcohol and acid, Parmukoff expressly leads one of skill away from the presently claimed invention.

Wenninger teaches that butylenes glycol is found in a number of skin care products. Wenninger further teaches that butylene glycol is a viscosity increasing agent. Wenninger offers no teaching or suggestion that butylenes glycol functions is useful in a virucidal composition for the treatment of an inflammation or lesion.

The cited references alone, or in combination thus fail to teach or suggest the presently claimed invention. Moreover, by teaching the **necessary inclusion of an amphoteric or pseudoamphoteric** compound (Yu *et al.*), by teaching that glycolic acid is an **irritant of skin** and mucous membranes (Merck Manual), by teaching the **necessity of a halide salt** (Pamukoff), the combination of references expressly lead one of skill away from the presently claimed method. Accordingly the Examiner has failed to make his *prima facie* case and the rejection of claims 1-6, 9, 11-22, and 24-34 under 35 U.S.C. §103(a) should be withdrawn.

Claims 1, 7-8. 15, and 24 were rejected under 35 U.S.C. §103(a) as allegedly obvious in light of Bhatia *et al.* (1998) *In. J. Animal Sci.* 68(6): 518-520, taken with "Disinfectant Drugs" and Remington. According to the Examiner, Bhatia *et al.* allegedly teaches that 0.4 N hydrochloric acid is effective to kill cow pox virus. Disinfectant Drugs was cited as allegedly teaching that 15% or above isopropanol is effective a single medicinal ingredient for disinfecting contact lenses. Remington was cited as allegedly teaching that alcohol is a good pharmaceutical solvent. Applicants traverse.

The Examiner is reminded that the claims are drawn to:

> 1. A method for **treating an inflammation or lesion on a human or animal** in need of said treatment, wherein said inflammation or lesion is caused by a virus, said method comprising:
> **contacting said inflammation or lesion** with a virucidally effective amount of a composition consisting of a pharmaceutically acceptable

> carrier and a C1, a C2, or a C3 straight chain alcohol, or a C2, C3, or C4 diol having a concentration of 0.2 to 12.5% by volume in water, and a sufficient amount of an acid to adjust the pH of the composition a range from 2.45 to 4.6.

Thus, the recited formulation is compatible with application to the surface of an animal or human, particularly to an area of inflammation or lesion.

In contrast, Bhatia *et al.* teaches the use of certain agents as **disinfectants of animal storage facilities**.

> Goat-pox dreadly [sic] contagious disease, has been occurring sporadically through the country causing economic threat to g at husbandry. To formulate the control measures **a suitable disinfectant is needed for decontamination of goat premises** during goat-pox outbreak apart from other things. [emphasis added] (page 518, col. 1)

Bhatia *et al.* contacted virus ***ex vivo*** with hydrochloric acid and incubated the suspension for a period of time (*see, e.g.,* page 518, 2nd column). To determine if the virus was alive **after** incubation with the acid, the suspension was injected under the goats' skin. Bhatia *et al.* offers no teaching or suggestion or any disclosure whatsoever that hydrochloric acid can be used to as a virucide for the treatment of "an inflammation or lesion on a human or animal".

Moreover it is well recognized that hydrochloric acid is a skin irritant. Thus, HCl may well be expected to exacerbate inflammation or severity of a lesion.

The defects of Bhatia *et al.* are not remedied by "Disinfectant Drugs" or Remington. To the contrary, Disinfectant Drugs teaches away from the combination of isopropyl alcohol with other agents. As stated therein:

> This monograph applies to products in liquid or table form intended to be used to disinfect contact lenses. **The medicinal ingredients, their concentrations and their combinations in Category IV products are restricted to those specified in this monograph**.

Isopropanol is identified on page 43 in a Table labeled "**Single Medicinal Ingredients**". This reference then continues to state:

> The following **combinations are considered acceptable**. The lower limits for use as a single ingredient also apply when the ingredient is used in combination.
>
> i) Chlorhexidine and EDTA

ii) Alkyltriethanolammonium chloride and EDTA
iii) Chlorhexidine, Polyaminopropyl biguanide and EDTA
iv) Polyquaternium-1 and EDTA. [emphasis added] (page 43)

As indicated above, Disinfectant Drugs teaches that combinations of medicinal ingredients are restricted to those specified in that monograph. Isopropanol is identified as a "single medicinal ingredient". Isopropanol is not listed in the acceptable combinations of ingredients.

Thus, Disinfectant Drugs expressly teaches away from the combination of isopropanol and other medicinal ingredients.

Moreover, combination of Isopropanol with another ingredient such as HCL would render it unsatisfactory for its intended purpose as indicated in the monograph. Thus, per MPEP §2143.01, citing *In re Gordon*, 221 USPQ 1125 (Fed. Cir. 1984) the modification proposed by the Examiner is non-obvious.

The defects of Bhatia *et al.* and Disinfectant Drugs is not remedied by Remington.

As stated by the Federal Circuit:

> ("Thus, in cases involving new chemical compounds, **it remains necessary to identify some reason that would have led a** chemist **to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound**."). Third, the Supreme Court's analysis in KSR presumes that the record before the time of invention would **supply some reasons for narrowing the prior art universe to a "finite number of identified, predictable solutions,"** 127 S. Ct. at 1742. [emphasis added] (Eisai Co. v. Dr. Reddy's Laboratories, Ltd. __ USPQ2d ___ (Fed. Cir. 2008)

Remington, cited by the Examiner, simply discuses isopropanol as one of a large number of solvents including for example, water, acetone, glycerin, propylene glycol, and the like. The references cited by the Examiner offer no teaching or reasons for narrowing the prior art universe to a finite number of identified predictable solutions, and, as explained above, actually teaches away from the claimed combination.

Thus, the combination of Bhatia *et al.*, Disinfectant Drugs, and Remington does not lead to or render the claimed invention obvious. As explained above, Bhatia *et al.* teaches the use of concentrated HCl to disinfect animal (goat) premises. This reference does not teach the application of HCL to a region of inflammation or lesion on a human or animal. It is general knowledge that HCL is

a skin irritant. This reference does not teach that application of HCl to such a region will not exacerbate the inflammation, and this reference does not teach the combination of HCl with another medicinal ingredient. Disinfectant drugs expressly teaches away from the combination of isopropanol with other agents. Remington simply provides a laundry list of a large number of pharmaceutical solvents.

Accordingly the Examiner has failed to make his *prima facie* case and the rejections under 35 U.S.C. §103(a) should be withdrawn.

In view of the foregoing, Applicants believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. Should the Examiner seek to maintain the rejections, Applicants request a telephone interview with the Examiner and the Examiner's supervisor.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 769-3513.

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Respectfully submitted,

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